FACT SHEET
Healthcare Provider

Argininosuccinic Aciduria (ASA)

Description:
Argininosuccinic Aciduria (ASA) is one of the urea cycle disorders and is caused by the deficiency of the enzyme argininosuccinic acid lyase. It is an autosomal recessive condition. This deficiency prevents the conversion of argininosuccinic acid into arginine. Individuals with ASA also cannot convert waste nitrogen, in the form of ammonia, into urea. This causes the ammonia to build up in the person's blood. Hyperammonemia is especially toxic to the nervous system and can result in brain damage. Occasionally, an individual may inherit a milder form of the disorder in which ammonia accumulates in the bloodstream only during periods of illness or other stress.

Symptoms:
There are two clinical forms of ASA: neonatal and sub-acute or late forms. Symptoms of the neonatal form are severe hyperammonemia accompanied by lack of appetite, tachypnea, persistent vomiting, listlessness, seizures, coma, and hepatomegaly. Clinical features typically present 24 to 72 hours after the first protein feeding. There is a high mortality rate. Late-onset patients may present with developmental delay or non-specific mental retardation, and/or skin and hair abnormalities between a few months and years of age.

Incidence in General Population:
1:70,000 live births

Diagnosis:
Newborn screening—Tandem mass spectrometry (MS/MS) identifies (secondary) elevations in the amino acid citrulline. A second dried-blood-spot filter paper card may be requested by the Newborn Screening Laboratory if the initial screening result is above the normal range. Infants with presumptive positive screening (critical) results require prompt follow up. If this occurred, the clinician would be contacted by the Metabolic Treatment Center. When notified of these results, the clinician should immediately check on the clinical status of the baby and facilitate referral to the Metabolic Treatment Center. The Metabolic Treatment Center will provide consultation and assistance with diagnostic testing.

Situations That Risk Metabolic Decompensation:
General anesthesia should be used with caution in patients with this condition as it can cause hyperammonia.

Monitoring:
- Clinical observation is an important tool for monitoring patients with ASA. It is important for primary care provider and the Metabolic Treatment Center to develop an ongoing collaborative relationship in caring for these patients.
- Carefully assess infants presenting with unexplained vomiting, lethargy, rapid respirations with respiratory alkalosis, and hypothermia.
- Late onset patients may present with developmental delay, non-specific mental retardation, seizures, hepatomegaly, and/or skin and hair abnormalities, between a few months and years of age.

Treatment:

- Treatment may include a high-caloric, protein-restrictive diet, arginine supplementation to help complete the urea cycle, essential amino acid supplementation, ammonia scavenging drugs in some cases, and supplemental carnitine if patient has a secondary deficiency.
- Liver transplantation offers a partial correction of the enzyme deficiency and improved metabolic status.
- Patients must avoid fasting; during stressors, such as illness, they need to supplement with high carbohydrates, non-protein calories to avoid catabolism.
- When left untreated, brain damage, coma, and death will occur.
- Patients who survive the severe hyperammonemia episodes usually have mental retardation and neurological dysfunction.

Illness:

- Patients with ASA must be monitored closely during times of illness, especially infections. Stressors, such as fever, can cause the body to break down its own proteins and exceed the capacity of the abnormal urea cycle to dispose of the waste nitrogen by-products.
- A sick-day plan should be formulated with the Metabolic Treatment Center.
- During illness, it is recommended that the protein intake be further restricted or stopped and consumption of high carbohydrate drinks is advised in order to maintain hydration. The patient should be seen by his/her physician. (However, prolonged fasting can result in catabolism.)
- Should hospitalization be necessary, treatment may consist of medications that help the body dispose of nitrogen-containing wastes. Hemodialysis may be required to help rid the body of excess ammonia during extreme illness and severe hyperammonemia.
- Consult with the Metabolic Treatment Center within 24 hours of the onset of an illness or at the time of hospitalization.

Immunization:

Immunizations must be kept current.

Surgical/Surgical Procedures:

Major stresses, such as surgery or accidents, can be complicated for ASA patients. Extreme care is required to avoid problems during such periods.

Growth and Development:

- It is crucial to closely monitor ASA patients. Despite optimum treatment, they are prone to periodic bouts of hyperammonemia, which can be life threatening and damaging.
- There is a direct correlation between the length of time a patient is in hyperammonemic coma as a neonate and the neurologic complications, including mental retardation. While early diagnosis and treatment may be lifesaving, neurologic damage is not usually prevented.
- In some patients, chronic hepatic dysfunction results in cirrhosis and liver failure, and a liver transplant may be indicated despite adequate treatment and metabolic control.

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